Entanglement Swapping Model of DNA Replication

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Molecular biology explains function of molecules by their geometrical and electronical structures that are mainly determined by utilization of quantum effects in chemistry. However, further quantum effects are not thought to play any significant role in the essential processes of life. On the contrary, consideration of quantum circuits/protocols and organic molecules as software and hardware of living systems that are co-optimized during evolution, may be useful to overcome the difficulties raised by biochemical complexity and to understand the physics of life. In this sense, we review quantum information-theoretic approaches to the process of DNA replication and propose a new model in which 1) molecular recognition of a nucleobase is assumed to trigger an intrabase entanglement corresponding to a superposition of different tautomer forms and 2) pairing of complementary nucleobases is described by swapping intrabase entanglements with interbase entanglements. We examine possible biochemical realizations of quantum circuits/protocols to be used to obtain intrabase and interbase entanglements. We deal with the problem of cellular decoherence by using the theory of decoherence-free subspaces and subsystems. Lastly, we discuss feasibility of the computational or experimental verification of the model and future research directions.

I. INTRODUCTION

According to the central dogma of molecular biology, genetic information stored in double-stranded DNA (dsDNA) is duplicated by replication of two strands independently. At each step of the replication, enzyme DNA polymerase (DNA*pol*) first recognizes the nucleobase (N = {A, T, G, C}) of the template DNA strand. Then, it finds complementary of this base ($\bar{\mathrm{N}}$ = {$\bar{\mathrm{A}}$=T, $\bar{\mathrm{T}}$=A, $\bar{\mathrm{G}}$=C, $\bar{\mathrm{C}}$=G}) from the surrounding environment and facilitates pairing of these bases through two or three interbase hydrogen bonds. A new dsDNA is synthesized from an existing single-stranded DNA (ssDNA) by successive pairings of the all nucleobases in this way.

Conformational changes occurring within DNA*pol* at each stage of the replication were demonstrated in detail by crystallization experiments [38]. Also, all possible interactions between amino acid side chains (that are likely to be found in the active site of DNA*pol*) and unpaired nucleobases were obtained by quantum chemical calculations [7]. However, there are still some unclear points about the relation of the high fidelity of replication process with the base recognition, searching, and pairing mechanisms [38]. Since active site of DNA*pol* that contribute to these mechanisms has a particularly complex structure involving a lot of amino acids [38], both experiments and quantum chemical calculations are still insufficient to clarify these mysteries. Thus, until the development of more sensitive setups and more sophisticated calculations, information processing models could be useful tools for a better understanding of DNA replication.

During the DNA replication, newly synthesized strands elongate with a rate 3,000 nucleotide per minute in humans [45] and 30,000 nucleotide per minute in bacteria [32]. Neither DNA binding nor nucleotide binding to the DNA*pol* limits this rate, they are very fast steps [14, 15, 38]. Also, replication without proofreading and repair mechanisms occurs with an error rate of 10^{-4} to 10^{-6} per nucleotide [32]. Such an accuracy can be within the constraints of quantum coherent information processing. Estimations based on both theoretical models [58] and experimental data [1, 3] give sufficiently long decoherence times for the coding nucleobase protons of dsDNA [31]. Thus, quantum information processing descriptions are expected to be explanatory models of DNA replication.

To understand the underlying mechanisms of DNA replication several quantum information processing models were proposed. For example, Patel [35] formulated nucleotide selection from surrounding environment as an unsorted database search. He examined the pertinence of Grover's algorithm [16] to give an explanation for the number of deoxyribonucleotide types used in dsDNA. Although he successfully modeled base pairing as oracle of the algorithm [35] and associated this model with the evolution of the triplet genetic code [36], initiation of the search in his model requires the symmetric quantum superposition of four disparate nucleotides which is not quite possible. Wave analogue [37] of this quantum search algorithm in which symmetric superposition state is replaced by the center-of-mass mode is more realistic for enzyme activity. However, if this version of the algorithm [37] is adopted for the activity of DNA*pol*, each base pairing should begin with the loading of DNA*pol* with four different free nucleotides before attempting to bind to DNA which is contrary to the present knowledge [14, 15, 38].

Recently, Cooper [9, 10] modeled base recognition mechanism in replication (and transcription) to understand time-dependent DNA mutations and A·T richness of DNA. To explain the stability of base pairs, he as-

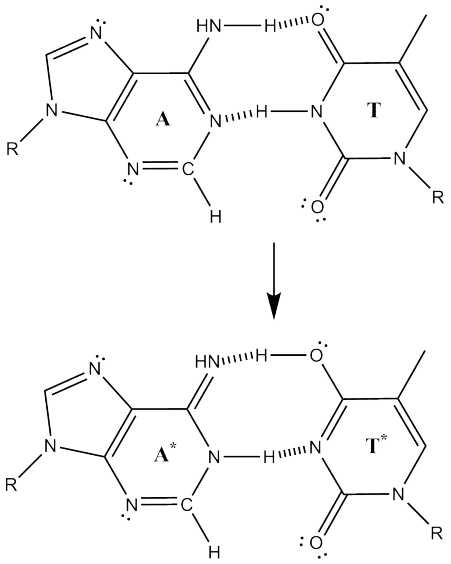

FIG. 1: A·T→A*·T* tautomeric transition which can be observed [26, 27, 50, 52, 54] in dsDNA.

sumed that interbase hydrogen bonds are rearranged by sequential intermolecular and intramolecular proton tunnelings. In this assumption, interbase tunnelings turn bases into their unusual tautomers (N* and N♯ in Figures 1, 2) pair-by-pair. Then, intramolecular tunnelings introduce coherent superposition states in which enol and imine protons of unusual tautomers are shared between two electron lone pairs that belong to a single atom. In the recognition step of the model, enzyme transcriptase (RNA-dependent DNA*pol*) makes quantum measurements on the coherent states of protons that are present on Watson-Crick (WC) edge (Figure 3). Although this model is compatible with molecular genetic transcription data of bacteriophage T4, some possible results of the transcriptase measurements, such as the decohered states corresponding to tautomers $G^{\sharp}_{002}$ and $G^{\sharp}_{000}$ [9, 10] do not generate information for any usual tautomer form: technically, qubit representation of a nucleobase was considered as the tensor product of states corresponding to the presence or absence of each WC edge proton. Then, Hilbert space should be 8-dimensional, but four bases states, that do not correspond to common tautomers, give no meaningful information to the enzyme. Therefore, in such situations where the result of the measurement is one of these spurious states, enzyme can not recognize the nucleotide base of DNA. This expresses an efficiency problem in both recognition and searching mechanisms.

II. ENTANGLEMENT SWAPPING MODEL OF REPLICATION

Estimation of long decoherence times for the WC edge protons [31] suggests that nontrivial quantum effects can

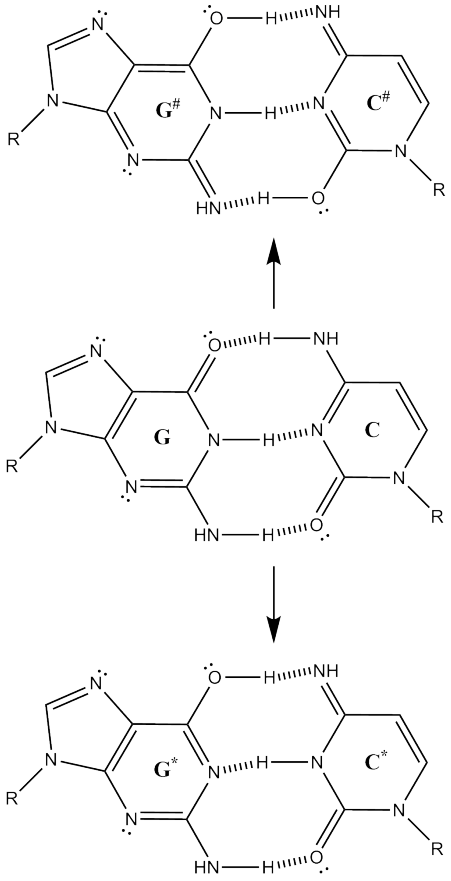

FIG. 2: G·C→G♯·C♯ and G·C→G*·C* tautomeric transitions which can be observed [12, 26, 51, 53] in dsDNA.

be involved in DNA replication. It is easy to show that the fastest quantum search algorithm [16, 57] is only four times faster than the slowest classical search algorithm for the case of searching complementary nucleotides of template bases. Therefore, if quantum coherence is maintained during replication, this should have been evolved to increase not only the speed, but also the accuracy. In this sense, our model is motivated to investigate quantum effects increasing both speed and accuracy together in the DNA replication.

A. Intrabase and Interbase Entanglements

During the DNA replication process free nucleotide binds to a solvent exposed pocket within DNA*pol* before base pairing, whereas template base is flipped out of the helix axis and into the active site [38]. Additionally, it is theoretically known that interaction with water molecules can induce transitions to rare tautomer forms [13]. Such higher energetic states can also be mediated by interactions with carboxylate and sodium ions [42] which are likely to be found both in the solvent exposed pocket and active site of the enzyme. Thus, tautomeric transitions are likely in both incorporated nucleobase and

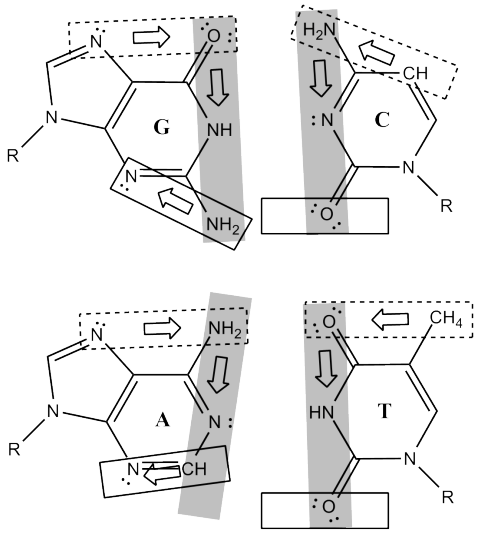

FIG. 3: Parts of the nucleobases: atoms can be grouped according to region they will be found in DNA. Hoogsteen (↔major groove), Watson-Crick (↔pairing plane), and Sugar (↔minor grove) edges are indicated respectively by dashed, filled, and plain boxes. Arrows inside the boxes show the order of the qubits used in qubit representation.

template base after recognition and before base pairing.

In this work, molecular recognition of a nucleobase is assumed to trigger a superposition of different tautomer forms, i.e. $|\mathrm{N}\rangle_{WC,I} \rightarrow |\mathrm{N}\rangle_{WC,Q} = \sum_t \alpha^t |\mathrm{N}^t\rangle_{WC}$ ($t = \{\ , *, \sharp\}$). Nucleobases A and T have two different tautomer forms, whereas G and C have three different tautomer forms in allowed transitions (Figures 1, 2). Superposition state $|\mathrm{N}\rangle_{WC,Q} = \alpha|\mathrm{N}\rangle_{WC} + \alpha^*|\mathrm{N}^*\rangle_{WC}$ requires the entanglement of first two WC edge atoms of nucleobase, whereas $|\mathrm{N}\rangle_{WC,Q} = \alpha|\mathrm{N}\rangle_{WC} + \alpha^*|\mathrm{N}^*\rangle_{WC} + \alpha^\sharp|\mathrm{N}^\sharp\rangle_{WC}$ requires the entanglement of all the three WC edge atoms. So, superposition of usual and unusual tautomer forms corresponds to an intrabase entanglement of WC edge atoms of the nucleobase. Such interbase entanglements will be invariant in the situations causing tautomeric transitions. Thus, formation of intrabase entanglements increase the speed of replication if they are not fragile to cellular decoherence.

Possible quantum mechanical transitions A·T→A*·T*, G·C→G$^\sharp$·C$^\sharp$ and G·C→G*·C* were found in dsDNA by density functional theory (DFT) calculations [50–54]. Hence, after base pairing, nucleobase pairs can exist in a superposition of states corresponding to different tautomer pairs, i.e. $|\mathrm{N}\cdot\bar{\mathrm{N}}\rangle_{WC,O} = \sum_t \beta^t |\mathrm{N}^t\cdot\bar{\mathrm{N}}^t\rangle_{WC}$ ($t = \{\ , *, \sharp\}$). However, probability amplitudes for unusual tautomer pairs (β^* and $\beta^\sharp$) are expected to be very small, since transitions to unusual tautomer pairs are very rare in dsDNA. Also, nonlocal DFT methods [17–19, 47] showed that minimum covalent contribution to the interbase hydrogen bonds is 38% in A·T pairing and is 35% in G·C pairing. This can be interpreted as quantum mechanical sharing of proton which causes an entanglement between the donor and acceptor atoms. In this view, superposition states $|\mathrm{N}\cdot\bar{\mathrm{N}}\rangle_{WC,O}$ produced by the base pairing correspond to interbase entanglements.

We propose that recognition triggers two two-particle entanglements in the $|\mathrm{N}\rangle_{WC,Q}$ states of A and T and two three-particle entanglements in the $|\mathrm{N}\rangle_{WC,Q}$ states of G and C (Figure 4). If we consider each interbase hydrogen bond as a two-particle entanglement, there are two two-particle entanglements in $|\mathrm{A}\cdot\mathrm{T}\rangle_{WC,O}$ state and three two-particle entanglements in $|\mathrm{G}\cdot\mathrm{C}\rangle_{WC,O}$ state after base pairing. In order to turn intrabase entanglements into interbase entanglements, recognition should be followed by an irreversible transformation. Therefore, in our model, base pairing is described by a multiparticle entanglement swapping [4] in which DNA*pol* swaps intrabase entanglements with interbase entanglements (Figure 4).

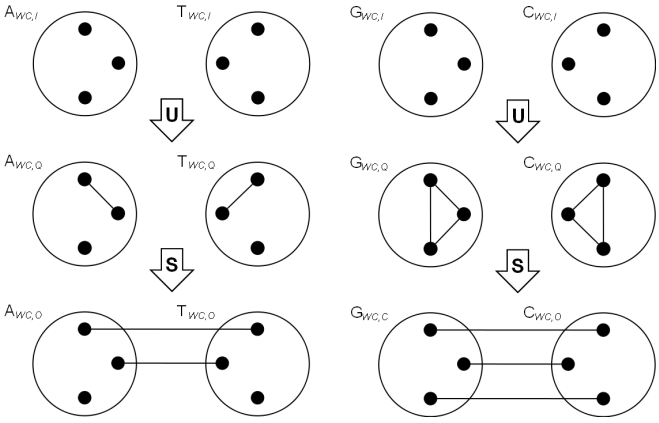

FIG. 4: Entanglement swapping model of replication. Each circle represents the WC edge of related nucleobase. Atoms on WC edge are shown by small dark points. A line linking two of such points means that there is an entanglement between the atoms shown by these points. Recognition process is described by a unitary transformation **U**: $|\mathrm{N}\rangle_{WC,I} \rightarrow |\mathrm{N}\rangle_{WC,Q}$, whereas base pairing is described by an irreversible transformation **S**: $|\mathrm{N}\rangle_{WC,Q} \rightarrow |\mathrm{N}\rangle_{WC,O}$

While van der Waals interactions between nucleotide bases in ssDNA were modeled by entanglement in a recent study [40], present study is the first example of modeling hydrogen bonds by entanglement and using (multiparticle) entanglement swapping in living systems. Intuitively, biomolecules appear to be classical objects since their de Broglie wavelengths are comparatively smaller than their actual size due to their huge molecular mass and high temperature. However, it is both theoretically and experimentally shown that entanglement can occur in macroscopic and hot non-equilibrium systems, such as biological ones [2, 5, 48, 49].

B. Qubit Representation of Input and Output Nucleotide States in Replication

Recognition process requires formation of at least two hydrogen bonds between amino acid side-chains of the DNA*pol* and nucleobase [7, 43]. Such pairs of hydrogen bonds can occur over one of the three parts of nucleotides [7] shown in Figure 3. In consensus, hydrogen bond donor and acceptor atoms of bases are only O and N atoms. However, there are a small number of computational observations in which C atoms of nucleotide bases have the ability to make blue-shifting hydrogen bonds [27]. In this respect, when electronic configurations of the individual O, N, and C atoms on Hoogsteen (H), Watson-Crick (WC), and Sugar (S) edges (Figure 3) are considered, it is found that each atom has two different energy states: a relatively lower energy state as acceptor and a relatively higher energy state as donor (Figure 5). These lower and higher energy states can be regarded as qubits $|0\rangle$ and $|1\rangle$, respectively (Figure 5). Then, reliable qubit representations can be written down for all the three edges of each nucleobase (Table I).

TABLE I: Qubit representations of usual and unusual tautomer forms found in the allowed transitions (Figures 1, 2): $|0\rangle$ and $|1\rangle$ states are assigned according to the absence and presence of a proton that can be shared in a hydrogen bond and order of the qubits are determined as shown in Figure 3.

Tautomer form	$\|\mathrm{N}\rangle_H$	$\|\mathrm{N}\rangle_{WC}$	$\|\mathrm{N}\rangle_S$
A	$\|01\rangle$	$\|101\rangle$	$\|10\rangle$
A *	$\|00\rangle$	$\|011\rangle$	$\|10\rangle$
T	$\|10\rangle$	$\|010\rangle$	$\|0\rangle$
T *	$\|11\rangle$	$\|100\rangle$	$\|0\rangle$
G	$\|00\rangle$	$\|011\rangle$	$\|10\rangle$
G *	$\|01\rangle$	$\|101\rangle$	$\|10\rangle$
G $^\sharp$	$\|01\rangle$	$\|110\rangle$	$\|00\rangle$
C	$\|11\rangle$	$\|100\rangle$	$\|0\rangle$
C *	$\|10\rangle$	$\|010\rangle$	$\|0\rangle$
C $^\sharp$	$\|10\rangle$	$\|001\rangle$	$\|1\rangle$

C. Quantum Aspect of the Enzyme Action

If states of the nucleobases which are measured by DNA*pol* live in a Hilbert Space whose dimension is larger than the number of these states, there can be unavoidable efficiency problems in both recognition and searching mechanisms. Also, states corresponding to usual tautomer forms should be orthogonal to each other. Under these conditions, DNA*pol* should recognize bases in both free nucleotide and ssDNA cases only over the H edge according to Table I. It is known that sequence-specific dsDNA binding proteins usually interact with the major groove [41] and so, they recognize nucleobases of dsDNA

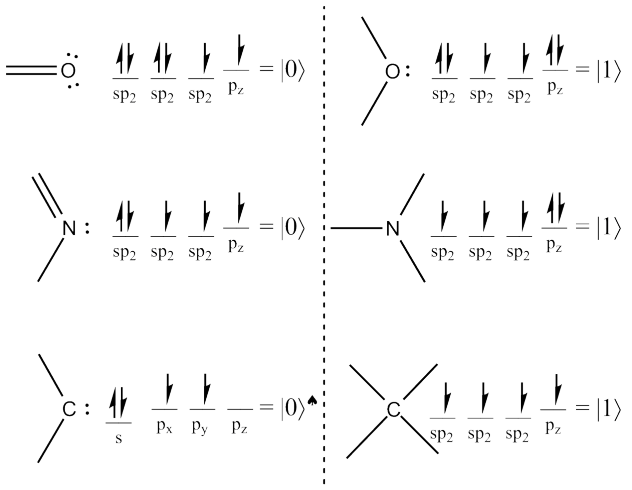

FIG. 5: Electronic configurations and qubit representations of the O, N, and C atoms: higher energy state $|1\rangle$ (lower energy state $|0\rangle$) corresponds to the presence (absence) of a proton which is bonded to that atom and which participates in interbase hydrogen bonds (Figures 1, 2). Configuration indicated by ♠ is not present in any tautomer form. However, it is possible to observe it in blue-shifting hydrogen bonds of DNA.

over the H edge, too. Such a coincidence is not a surprise, since reading information from dsDNA and ssDNA by different proteins ought to be based on similar principles.

If DNA*pol* makes a quantum measurement on the state $|\mathrm{N}\rangle_H$ to recognize a nucleobase, first qubit gives information about purine-pyrimidine distinction, whereas the second one gives information about imino-enol distinction. In this sense, DNA*pol* should pair bases whose qubit representations are complementary to each other (see Table I). Not only correct base pairings, but also mispairings like A·C* and G*·T can be accounted for by this assumption.

A quantum measurement requires an entanglement between the measuring device and measured system. In this case, it can be considered as a hydrogen bonding between the DNA*pol* and the nucleobase. Also, it is reasonable to assume that entanglement between the DNA*pol* and the nucleobase should be maximal since an accurate measurement requires strong coupling between measuring device and measured system.

Hypothetically, a proton transfer between the DNA*pol* and the second atom of H edge (or equally the first atom of WC edge) which occurs during the recognition, can trigger a tautomeric transition (Figure 6). Since such a transfer has a quantum nature in a hydrogen bonding, recognition can trigger a transition to the superposition of usual and unusual tautomer forms by a unitary transformation $\mathbf{U}$. This mechanism is a toy model of evolution of the basis states $|\mathrm{N}\rangle_{WC,I}$ (Table I) into superposition states $|\mathrm{N}\rangle_{WC,Q} = \sum_t \alpha^t |\mathrm{N}^t\rangle_{WC,I}$ ($t = \{\ , *, \sharp\}$) as fol-

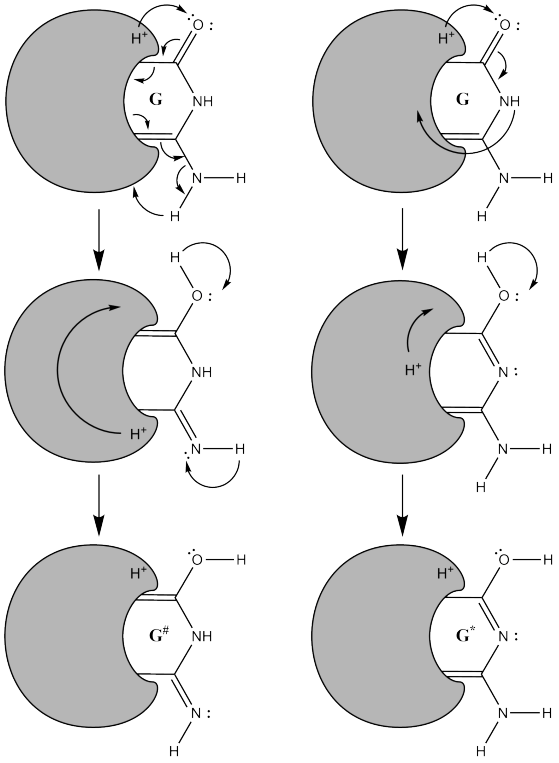

FIG. 6: An hypothetical mechanism for the tautomeric transitions of nucleobase G by proton transfer between enzyme DNA*pol* and nucleotide. Grey structure represents the active site of DNA*pol* and arrows show proton and electron delocalizations.

lows:

$$
\begin{aligned}
|\mathrm{A}\rangle_{WC,I} \xrightarrow{\mathrm{U}} |\mathrm{A}\rangle_{WC,Q} &= a|101\rangle + a^*|011\rangle\,, \qquad (1)\\
|\mathrm{T}\rangle_{WC,I} \xrightarrow{\mathrm{U}} |\mathrm{T}\rangle_{WC,Q} &= t|010\rangle + t^*|100\rangle\,,\\
|\mathrm{G}\rangle_{WC,I} \xrightarrow{\mathrm{U}} |\mathrm{G}\rangle_{WC,Q} &= g|011\rangle + g^*|101\rangle + g^\sharp|110\rangle\,,\\
|\mathrm{C}\rangle_{WC,I} \xrightarrow{\mathrm{U}} |\mathrm{C}\rangle_{WC,Q} &= c|100\rangle + c^*|010\rangle + c^\sharp|001\rangle\,.
\end{aligned}
$$

Now, it is clearly seen that these superpositions of different tautomer forms are nothing else than intrabase entanglements of the atoms on WC edge. Nucleobases A and T have two different tautomer forms, whereas G and C have three different tautomer forms in allowed transitions (Figures 1, 2). Thus, after recognition, we observe two two-qubit entanglements in the states of A and T, while there are two three-qubit entanglements in the states of G and C (Figure 4).

Recognition process of complementary nucleobase $\bar{\mathrm{N}}$ also involves a quantum measurement in which a maximal entanglement is formed between DNA*pol* and $\bar{\mathrm{N}}$. However, DNA*pol* can not bind to $\bar{\mathrm{N}}$ in such a quantum mechanical way until it disentangles itself from N. This is because of the entanglement monogamy (or polygamy) [6, 8, 24] which roughly says that if A and B are maximally entangled, then any one of them can not be simultaneously entangled with C. In the context of monogamy, formation of intrabase entanglement in N breaks the maximal entanglement between DNA*pol* and N. Then, a maximal entanglement between DNA*pol* and $\bar{\mathrm{N}}$ becomes possible.

Similarly, recognition of $\bar{\mathrm{N}}$ induces an intrabase entanglement in $\bar{\mathrm{N}}$ which disentangles DNA*pol* from $\bar{\mathrm{N}}$. This disentanglement allows DNA*pol* to bond N and $\bar{\mathrm{N}}$ together and then to bind to the subsequent N of ssDNA in a quantum mechanical way. Therefore, formation of intrabase entanglements not only prevents the uncontrollable tautomeric transitions caused by cellular environment, but also provides separation of DNA*pol* from one nucleotide and binding of it to another.

After base pairing, nucleobase pairs should exist in a superposition of states corresponding to different tautomer pairs. Since state of a hydrogen bonded atom pair can be written as the Bell state $|\beta_{01}\rangle = (|01\rangle + |10\rangle)/\sqrt{2}$, these superposition states $|\mathrm{N}_1 \cdot \bar{\mathrm{N}}_2\rangle_{WC,O}$ are actually interbase entanglements. Therefore, it can be said that in the case of G·C pair, there are three two-qubit entanglements in $|\beta_{01}\rangle$ state, and in the case of A·T pair, there are two two-qubit entanglements in $|\beta_{01}\rangle$ state. In order to turn intrabase entanglements into interbase entanglements, **U** should be followed by an irreversible transformation **S**. Thus, in our model, base pairing occurs as a multiparticle entanglement swapping in which DNA*pol* swaps intrabase entanglements with interbase entanglements (Figure 4).

D. Quantum Circuit for Intrabase Entanglement

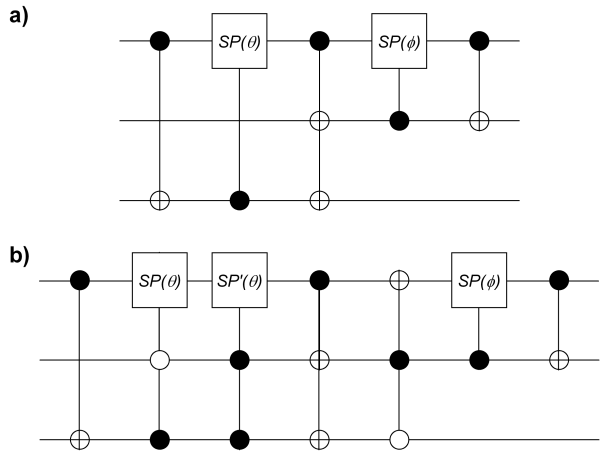

FIG. 7: Two of the possible quantum circuits for transformation **U** which turns $|\mathrm{N}\rangle_{WC,I}$ states into the $|\mathrm{N}\rangle_{WC,Q}$ states. Superposition matrices $SP(\theta)$ and $SP'(\theta)$ of *controlled − Superposition* gates equals to the multiplication of rotation matrix $R(\theta)$ and Pauli-Z matrix with different orders: $SP(\theta) = R(\theta) \times Z$ and $SP'(\theta) = Z \times R(\theta)$.

Two candidates for the transformation **U** are shown in the Figure 7. To provide a decoherence-free (DF) sub-

system [21, 23, 29, 30], we take the angles θ and ϕ in the second quantum circuit (Figure 7-b) as $\arccos(\sqrt{1}/\sqrt{3})$ and $\arccos(1/\sqrt{2})$, respectively. Then, $|\mathrm{N}\rangle_{WC,Q}$ states are obtained as:

$$
\begin{aligned}
|\mathrm{A}\rangle_{WC,Q} &= (+|011\rangle - |101\rangle)/\sqrt{2}\,, \\
|\mathrm{T}\rangle_{WC,Q} &= (+|010\rangle - |100\rangle)/\sqrt{2}\,, \\
|\mathrm{G}\rangle_{WC,Q} &= (+|011\rangle + |101\rangle - 2|110\rangle)/\sqrt{6}\,, \\
|\mathrm{C}\rangle_{WC,Q} &= (-|100\rangle - |010\rangle + 2|001\rangle)/\sqrt{6}\,.
\end{aligned}
\tag{2}
$$

To consider each base pair as an intact system, tensor products of these states should be taken.

$$
\begin{aligned}
|\mathrm{A}\otimes\mathrm{T}\rangle_{WC,Q} = \frac{1}{2}(&|011\rangle|010\rangle + |011\rangle|100\rangle \\
&- |101\rangle|010\rangle + |101\rangle|100\rangle)\,,
\end{aligned}
\tag{3}
$$

$$
\begin{aligned}
|\mathrm{G}\otimes\mathrm{C}\rangle_{WC,Q} = \frac{-2}{\sqrt{3}}(&\frac{|011\rangle|100\rangle}{4} + \frac{|101\rangle|100\rangle}{4} - \frac{|110\rangle|100\rangle}{2} \\
&+ \frac{|011\rangle|010\rangle}{4} + \frac{|101\rangle|010\rangle}{4} - \frac{|110\rangle|010\rangle}{2} \\
&- \frac{|011\rangle|001\rangle}{2} - \frac{|101\rangle|001\rangle}{2} + |110\rangle|001\rangle)\,.
\end{aligned}
$$

We reorder qubits of these product states in such a way that hydrogen bonded atom pairs come next to each other in order to clarify base pairing. Then, we get

$$
\begin{aligned}
|\mathrm{A}\cdot\mathrm{T}\rangle_{WC,Q} = \frac{1}{2}(&|00\rangle|11\rangle|10\rangle + |01\rangle|10\rangle|10\rangle \\
&- |10\rangle|01\rangle|10\rangle + |11\rangle|00\rangle|10\rangle)\,,
\end{aligned}
\tag{4}
$$

$$
\begin{aligned}
|\mathrm{G}\cdot\mathrm{C}\rangle_{WC,Q} = \frac{-2}{\sqrt{3}}(&\frac{|01\rangle|10\rangle|10\rangle}{4} + \frac{|11\rangle|00\rangle|10\rangle}{4} - \frac{|11\rangle|10\rangle|00\rangle}{2} \\
&+ \frac{|00\rangle|11\rangle|10\rangle}{4} + \frac{|10\rangle|01\rangle|10\rangle}{4} - \frac{|10\rangle|11\rangle|00\rangle}{2} \\
&- \frac{|00\rangle|10\rangle|11\rangle}{2} - \frac{|10\rangle|00\rangle|11\rangle}{2} + |10\rangle|10\rangle|01\rangle)\,.
\end{aligned}
$$

E. Swapping Protocol for Interbase Entanglement

Swapping intrabase entanglements to interbase entanglements can be achieved by a three-step protocol **S** as follows:

1. Reordered base pair states are subjected to a transformation V as shown in Figure 12. Then, fifth and sixth qubits of the G·C (or C·G) pair become $|01\rangle$, whereas fifth and sixth qubits of the A·T (or T·A) pair become $|11\rangle$. After this transformation, any improper base pair exists in a superposition of states in which third qubit pair is always $|00\rangle$ or $|10\rangle$.

2. If the sixth qubit is $|0\rangle$, first and second qubit pairs undergo a transformation A as shown in Figure 9-a. Otherwise, these qubit pairs are transformed with transformation B (Figure 9-b). Then, first and second qubit pairs of proper base pairs collapse into Bell state $|\beta_{01}\rangle = (|01\rangle + |10\rangle)/\sqrt{2}$, whereas first and second qubit pairs of improper base pairs collapse into Bell state $|\beta_{11}\rangle = (|01\rangle - |10\rangle)/\sqrt{2}$.

3. Firstly, fifth qubit is passed through a *Hadamard* (H) gate. Then, sixth qubit is converted by *NOT* (X) gate if the fifth qubit is $|1\rangle$. After this step, third qubit pair of the G·C (or C·G) pair becomes $|\beta_{01}\rangle$, whereas third qubit pair of the A·T (or T·A) pair becomes $|\beta_{11}\rangle$. In contrast, fifth and sixth qubits of any improper base pair exists in one of the Bell states $|\beta_{00}\rangle = (|00\rangle + |11\rangle)/\sqrt{2}$ or $|\beta_{10}\rangle = (|00\rangle - |11\rangle)/\sqrt{2}$.

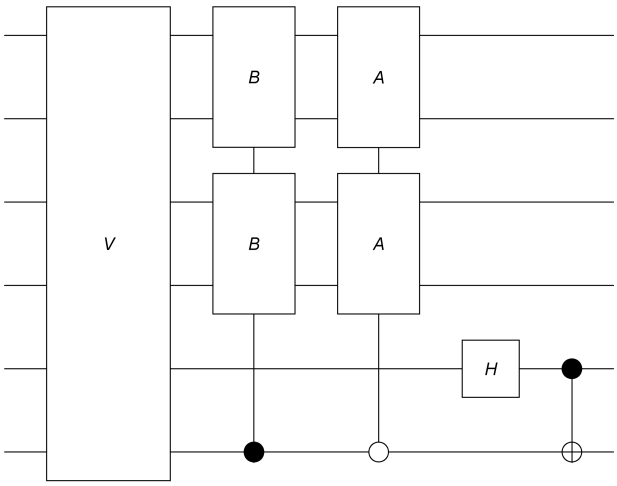

FIG. 8: Quantum circuit for **S** which swaps intrabase entanglements to interbase entanglements: H is the *Hadamard* gate which equals to $SP(\pi/4)$ defined in Figure 7. Transformations A and B are shown in the subsequent figure. See Appendix for the details of transformation V.

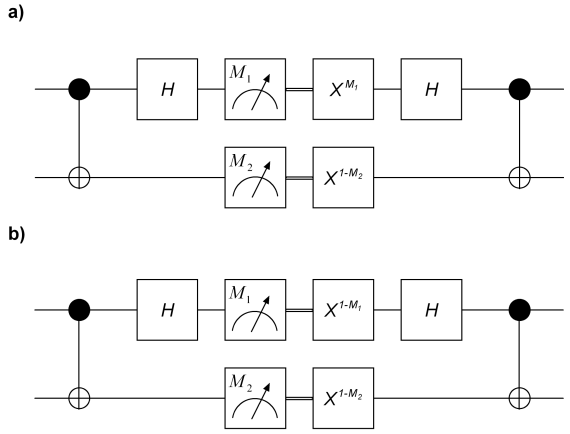

FIG. 9: Quantum transformations A and B used in **S**: they are actually modified Bell measurements. Modifications made by X which is the *NOT* gate (or Pauli-X gate) and X's superscript (M_1 or M_2) is the outcome of the measurement which is done immediately before it. *a*) A transforms any Bell state $|\beta_{ij}\rangle$ into the Bell state $|\beta_{11}\rangle$. *b*) B transforms any Bell state $|\beta_{ij}\rangle$ into the Bell state $|\beta_{01}\rangle$.

Immediately after **S**, proper $|\mathrm{N}_1\cdot\bar{\mathrm{N}}_2\rangle_{WC,O}$ states are

written in terms of the Bell states as follows.

$$|\mathrm{A}\cdot\mathrm{T}\rangle_{WC,O}=|\mathrm{T}\cdot\mathrm{A}\rangle_{WC,O}=|\beta_{01}\rangle|\beta_{01}\rangle|\beta_{11}\rangle, \quad (5)$$
$$|\mathrm{G}\cdot\mathrm{C}\rangle_{WC,O}=|\mathrm{C}\cdot\mathrm{G}\rangle_{WC,O}=|\beta_{01}\rangle|\beta_{01}\rangle|\beta_{01}\rangle.$$

F. Biochemical Realizations of Quantum Circuits/Protocols

Pauli-X transformation of controlled-NOT gates used in the quantum circuit of $\mathbf{U}$ (Figure 7-b) converts $|1\rangle_N$ into $|0\rangle_N$. When state of the DNA*pol* is also considered with the subscript E, this transformation should be $|1\rangle_N|0\rangle_E \rightarrow |0\rangle_N|1\rangle_E$. Since $|0\rangle$ and $|1\rangle$ states of an atom respectively correspond to the absence and presence of a proton bonded to that atom, this transformation can be regarded as a proton tunneling from the nucleobase to DNA*pol* through the atom on which the gate acts. Vice versa is possible for the action of Pauli-X transformation on the state $|0\rangle_N$.

Other gates used in the quantum circuit of $\mathbf{U}$ are controlled-SP and -SP' gates. When argument of SP transformation equals to $\arccos(1/\sqrt{2})$, it transforms $|0\rangle_N$ into $(|0\rangle+|1\rangle)/\sqrt{2}$ and $|1\rangle_N$ into $(|0\rangle-|1\rangle)/\sqrt{2}$. The former transformation should be $|0\rangle_N|1\rangle_E \rightarrow |\beta_{01}\rangle_{NE}$ by taking into account also the state of DNA*pol*, whereas the latter transformation should be $|1\rangle_N|0\rangle_E \rightarrow |\beta_{11}\rangle_{NE}$. So, the action of the SP transformation on the state $|0\rangle_N$ can be considered as formation of a hydrogen bond between the nucleobases and enzyme through the atom on which gate acts. On the contrary, an antibonding should occur by the action of SP transformation on the state $|1\rangle_N$. This is because of the fact that free energy in the state $|\beta_{11}\rangle_{NE}$ is greater than the one in which there is no interaction. Since entanglement measure of the generated state changes when the argument is changed, action of SP transformation can produce bondings/antibondings with different strengths for different arguments. Action of SP' transformation on $|0\rangle_N$ produces the same state as the SP action on $|1\rangle_N$ and vice versa. Thus, action of SP' transformation can be also considered as bondings/antibondings.

Both the proton transfer and hydrogen bonding are the usual tasks done by enzymes and there are some evidences for the unignorable role of quantum effects and dynamics on the enzymatic reactions [25, 28, 44]. Therefore producing an intrabase entanglement by transformation $\mathbf{U}$ is a possible action performed by the enzyme DNA*pol* (Figure 10).

Besides $\mathbf{U}$, swapping protocol $\mathbf{S}$ also includes controlled-NOT, -SP, and -SP' gates which are regarded as respectively proton tunneling and hydrogen bonding/antibonding between a nucleobase and DNA*pol*. Additionally, $\mathbf{S}$ contains swap gates (Figure 12) and modified Bell measurements (A and B). Swap gate exchanges the states of two qubits on which it acts: $|10\rangle \rightarrow |01\rangle$ and $|01\rangle \rightarrow |10\rangle$. So, it can be interpreted as a proton tunneling similar to interpretation of Pauli-X transformation of controlled-NOT gate. However, atoms on which swap gate acts can belong either to the same nucleobase or to the different nucleobases in the base pair. Hence, this proton tunneling should be considered inside a nucleobase or between the two different bases.

Outcome of the modified Bell measurement B is the

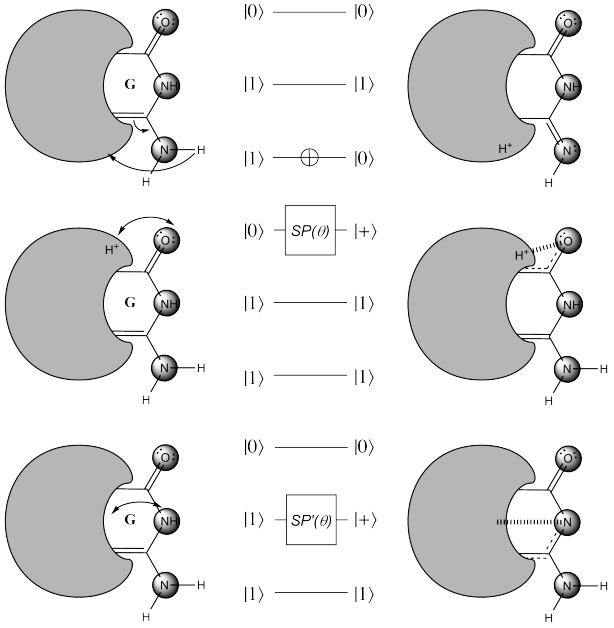

FIG. 10: Simple depictions of the actions of the NOT, SP, and SP' gates: atoms whose energy states are represented by qubits are the ones inside the shaded spheres. Evolution of the $|N\rangle_{WC}$ state of the nucleobase due to the action of gate is shown from left to right and $|+\rangle$ qubit equals to $(|0\rangle+|1\rangle)/\sqrt{2}$ if θ equals to $\arccos(1/\sqrt{2})$.

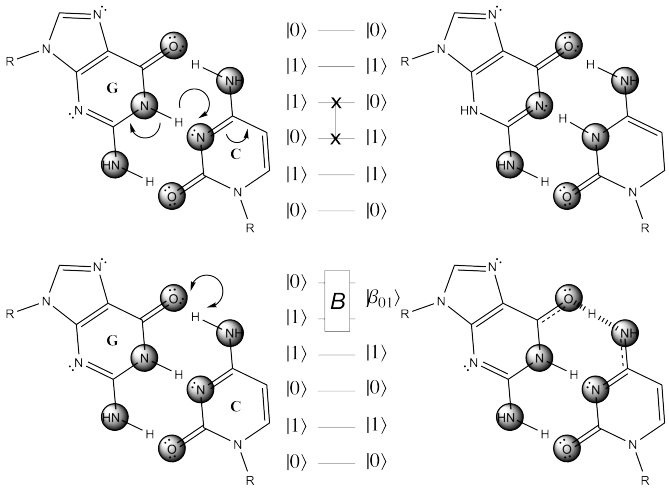

FIG. 11: Simple depictions of the actions of the swap gate and modified Bell measurement B: atoms whose energy states are represented by qubits are the ones inside the shaded spheres. Evolution of the reordered $|\mathrm{N}\cdot\bar{\mathrm{N}}\rangle_{WC}$ state of the nucleobase pair due to the action of gate is shown from left to right and $|\beta_{01}\rangle$ Bell state equals to $(|01\rangle+|10\rangle)/\sqrt{2}$.

Bell state $|\beta_{01}\rangle$, whereas the outcome of the modified Bell measurement A is the Bell state $|\beta_{11}\rangle$. Thus, these measurements can also be thought as a hydrogen bonding/antibonding. Contrary to the ones produced by SP and SP' gates, this bonding/antibonding is between the two nucleobases and its strength is always maximum. Consequently, **S** consists of nothing more than proton tunneling and hydrogen bondings/antibondings which are the usual tasks done by enzymes like DNA*pol* (Figures 10, 11).

Immediately after the entanglement swapping, states of proper base pairs are found as in Equation 5. According to these states, A·T (or T·A) base pair has two hydrogen bonds and G·C (or C·G) base pair has three hydrogen bonds as in the actual case. However, these hydrogen bonds have a maximum strength since Bell states are maximally entangled. Amplitudes in these states should change by the quantum evolution in the presence of the asymmetric double well potentials of the hydrogen bonded atom pairs. Thus, strengths of the hydrogen bonds should gradually decrease to the actual ones. Moreover, there is an antibonding between the last atom pair in A·T (or T·A). These atoms repulse each other because of the higher free energy of antibonding, but strength of this repulsion should also decrease by time. Since one of the atoms in this antibonding is C atom, final strength of the repulsion should be negligible.

On the other hand, both first and second atom pairs of the improper base pairs have an antibonding after the entanglement swapping. Final strength of the repulsions due to these antibonding interactions are not negligible and so, they should destabilize and separate the improper base pairs. However, state of the last atom pair in these base pairs are obtained as $|\beta_{00}\rangle$ or $|\beta_{10}\rangle$. Since total proton number of the base pair does not remain constant after collapsing to these states, atom pair and DNA*pol* can not separate from each other. In fact, these Bell states should be treated as an entanglement between the atom pair and DNA*pol* when state of the enzyme is also under consideration: $|00\rangle_{N\bar{N}} \pm |11\rangle_{N\bar{N}} \rightarrow |00\rangle_{N\bar{N}}|11\rangle_E \pm |11\rangle_{N\bar{N}}|00\rangle_E$. It can be that it is this entanglement which keeps DNA*pol* in place till the correct $\bar{\text{N}}$ comes along. Both of the asymmetric potentials and destabilization of the base pair should weaken this entanglement. When entanglement is weakened enough, DNA*pol* can bind to the correct $\bar{\text{N}}$ because of the converse monogamy [20] which roughly says that if A and B are weakly entangled, then any one of them could be strongly entangled with C. After that, a Pauli-X transformations can fix the total number of protons on the improper base pair and make incorrect $\bar{\text{N}}$ separable from the complex.

Neither **U** nor **S** is unique for the given model. However, this is not a disadvantage since there are several DNA*pol* species and families with different replication fidelities. This diversity in replication fidelity of DNA*pol* can be accomplished by different **U** and **S** pairs.

G. Effects of Cellular Decoherence

The intact system which is exposed to decoherence is the whole nucleobase - DNA*pol* complex. Hence, states of the nucleobases alone are not sufficient to determine if decoherence has a significant effect on the transformation **U** or does not. To draw a complete picture of interaction, assume that there are q hydrogen bond acceptors and $(k-q)$ hydrogen bond donors in the active site of DNA*pol*. If so, enzyme's active site can be represented by the state $|0\rangle_E^{\otimes q} \otimes |1\rangle_E^{\otimes(k-q)}$ after a proper ordering in which all $|0\rangle$ qubits are put to left of all $|1\rangle$ qubits. Then, we can obtain the initial state of the nucleobase - DNA*pol* complex as $|s\rangle_I = |\text{N}\rangle_{WC,I} \otimes |0\rangle_E^{\otimes q} \otimes |1\rangle_E^{\otimes(k-q)}$. Cellular decoherence effect on the state $|s\rangle$ can be simplified as a weak collective decoherence [21, 30] which turns $|1\rangle$ states into $e^{i\phi}|1\rangle$, while $|0\rangle$ states remain unchanged. Since we have already considered $|0\rangle$ and $|1\rangle$ states of an atom respectively as the absence and presence of a proton bonded to that atom, this simplification makes sense: decoherence can not affect an absent proton.

When spacing between the qubits is smaller than the wavelength of the radiation field which acts as a boson bath for the qubit system, collective decoherence dominates among the others [21, 29, 30]. In this sense, weak collective decoherence seems to be relevant not only to long-range electrostatic interactions with the intracellular ions, but also to short-living couplings with the thermal reservoir. Investigation of the effect of thermal reservoir on the internal DNA mobility requires a lattice dynamic approach based on an atomistic description of the molecule [56]. According to the appropriate methods given in [22, 55], maximum frequency of the vibrational modes in DNA is a few hundreds of cm^{-1} at room temperature. Corresponding phonon wavelength is in the order of μm and this is quite longer than the qubit spacing in our model, which is no more than $3\,\mathring{A}$. Thus, phonon bath can not distinguish the qubits and collective decoherence is expected to be the dominant decoherence mechanism in the DNA replication.

Defining a variable λ_K which equals to the number of $|0\rangle$ qubits minus the number of $|1\rangle$ qubits in a state over K qubits, [21, 30] showed that subspaces of Hilbert space spanned by the states with constant λ_K are decoherence-free (DF) during a collective dephasing process as described above. Then, a DF subspace for a specific λ_K is denoted as $DFS_K(\lambda_K)$ [21, 30].

In our model, there is no proton exchange between the system and its environment during the transformation **U**. For example, when a $|1\rangle$ qubit of nucleobase turns into $|0\rangle$ qubit after a controlled-NOT gate, a $|0\rangle$ qubit of DNA*pol* should also turn into $|1\rangle$ qubit, since Pauli-X transformation of controlled-NOT gate corresponds to a proton tunneling between the nucleobases and DNA*pol*. Therefore, value of the $\lambda_{K=3+k}$ remains fixed and transformation **U** does not take any state $|s\rangle$ out of the $DFS_{3+k}(2q-k+1)$ or $DFS_{3+k}(2q-k-1)$. This means that decoherence is

avoided during the formation of intrabase entanglements.

Each state that corresponds to an intrabase entanglement (Equations 1, 2) lives in one of the DF subspaces $DFS_3(+1) = \text{Span}\{|001\rangle, |010\rangle, |100\rangle\}$ and $DFS_3(-1) = \text{Span}\{|011\rangle, |101\rangle, |110\rangle\}$. However, intrabase entanglements should immune not only to the weak collective decoherence, but also to the strong collective decoherence: formation of the intrabase entanglement separates the recognized nucleobase from the DNA*pol*. This separation removes the isolation provided by the enzyme and exposes the nucleobase to the cellular environment. Assumption of the collective decoherence to be weak may lose its validity by the removal of the isolation. Thus, effects of the strong collective decoherence on the intrabase entanglements should also be investigated. These effects can be understood in terms of the actions of Pauli-X, -Y, and -Z transformations [21, 30]. 64×64 Pauli spin matrices transform intrabase entanglements as follows:

$$\begin{aligned} S_x : |\mathrm{N}\rangle_{WC,Q}|\bar{\mathrm{N}}\rangle_{WC,Q} &\rightarrow |\bar{\mathrm{N}}\rangle_{WC,Q}|\mathrm{N}\rangle_{WC,Q} \\ S_y : |\mathrm{N}\rangle_{WC,Q}|\bar{\mathrm{N}}\rangle_{WC,Q} &\rightarrow |\bar{\mathrm{N}}\rangle_{WC,Q}|\mathrm{N}\rangle_{WC,Q} \\ S_z : |\mathrm{N}\rangle_{WC,Q}|\bar{\mathrm{N}}\rangle_{WC,Q} &\rightarrow |\mathrm{N}\rangle_{WC,Q}|\bar{\mathrm{N}}\rangle_{WC,Q} \end{aligned} \quad (6)$$

Since transformation **S** produces same interbase entanglements from $|\mathrm{N}\rangle_{WC,Q}|\bar{\mathrm{N}}\rangle_{WC,Q}$ and $|\bar{\mathrm{N}}\rangle_{WC,Q}|\mathrm{N}\rangle_{WC,Q}$ states, effects of the strong collective decoherence on the intrabase entanglements seem to be trivial. This allows DNA*pol* to safely search for the complementary free nucleobase after the recognition of nucleobase of ssDNA and to safely continue pairing of bases after finishing the search.

Conservation of the proton number of nucleobase - DNA*pol* complex is trivial under the actions of swap gates and modified Bell measurements. Hence, decoherence suppression during and after the swapping protocol **S** can be demonstrated in a similar way as is done for the transformation **U**.

III. DISCUSSIONS

In the presence of strong collective decoherence, smallest DFS (DF subspace or subsystem) in which at least one qubit of information can be encoded is a three qubit subsystem $DFS_{K=3}(J = 1/2)$ [21, 30]. Construction of this subsystem involves the use of four three-particle $J = 1/2$ states. So, physical implementation of the computation inside the smallest DFS requires the use of four distinct building blocks each of which participates in the computation over three physical qubits. Number of orthogonal states living inside the smallest DFS imposes a restriction on the number of different building block types, whereas required qubit number for the computation inside the smallest DFS puts a limit on the atom number present in the interaction region of these building blocks.

Two of the four three-particle $J = 1/2$ states that are constructed by adding a two-particle $J = 0$ state to a one-particle $J = 1/2$ state imply the entanglements of first two physical qubits of the corresponding building blocks. Likewise, other two three-particle $J = 1/2$ states that are constructed by adding a two-particle $J = 1$ state to a one-particle $J = 1/2$ state imply the entanglements of all the three physical qubits of the remaining building blocks. Also, two states constructed by the same way should be associated in an appropriate way to encode a DF qubit. The conventional way of DF encoding inside the subsystem $DFS_{K=3}(J = 1/2)$ is taking the superpositions of these states. However, quantum superposition of the corresponding building blocks are unlikely to be formed. Pairing of the building blocks, whose entangled qubit numbers coincide, would be a more reasonable way in a biological sense. Such a pairing can be obtained by swapping intramolecular entanglements with intermolecular entanglements. Since first two of the four $J = 1/2$ states exclude the last physical qubits from the intramolecular entanglements, intermolecular entanglements obtained by the pairing of the corresponding building blocks should not include the entanglement of their last physical qubits. On the contrary, pairing of the other two building blocks should result in three intermolecular entanglements between them.

In fact, if single-particle $|j = 1/2, m_j = 1/2\rangle$ state is represented by $|0\rangle$ qubit, four three-particle $J = 1/2$ states are nothing else than the $|N\rangle_{WC,Q}$ states corresponding to intrabase entanglements. It would be interesting if we could bring the similarities between the discussed scenario and processing of genetic information beyond an analogy.

Although tens of nucleotide derivatives are found in nature, especially in tRNAs, genetic information is encoded by only four nucleotides in the dsDNA. These deoxyribonucleotides usually form Watson-Crick base pairs in which pairing occurs over the three WC edge atoms of the nucleobases (Figure 3): A and T form a pair through two interbase hydrogen bonds, whereas G and C form a pair through three interbase hydrogen bonds. The third atom in WC edge of adenine is a carbon atom which is responsible for the lack of one hydrogen bond in the A·T pair. Preference of the carbon rather than a more electronegative atom as the third WC edge atom of adenine may be a coincidental event stand out in the evolution of nucleobases. Such a restriction on both nucleobase types and interbase interactions used in the usual structure of the genetic information should have an explanation in the evolutionary basis.

One of the essential problems of any information processing in living systems is the presence of unavoidable noise. To survive, organisms must have some special computational strategies for coping with this problem. Since the nature of molecular realm is quantum mechanical, making computation inside noiseless DFS may be a favorable strategy. However, organisms must process information not only more accurately, but also more powerfully. So, any discovery of biological DF computation should have been followed by further optimizations on the use of resources like energy, time, and number of physical

building blocks. Such a resource optimization actually corresponds to a minimization of the qubit number required in the computation. In this sense, restriction on both nucleobase types and interbase interactions used in the usual structure of the genetic code may have been a result of the further resource optimization in biological DF computation.

IV. CONCLUSIONS

Since all of the steps in both **U** and **S** can be expressed as proton transfer and hydrogen bonding, the replication scenario proposed in our model could be tested step by step with the help of computational methods of quantum chemistry.

In addition to computational tests, some experimental setups may be designed to explore some of the predictions of the model. For example, states of base pairs immediately after the pairing are obtained as in Equation 5. Indeed, $|\mathrm{N}_1 \cdot \bar{\mathrm{N}}_2\rangle_{WC,O}$ states are superpositions of different tautomer forms with equal probability amplitudes. As discussed before, these amplitudes should change by the quantum evolution in the presence of the asymmetric double well potentials of the hydrogen bonded atom pairs until they reach the actual values. Then, it can be hypothesized that if this evolution can be prevented in a proper way, probability of point mutations due to the formation of rare tautomer forms should be higher than the ones obtained *in vivo*. This may be achieved by sufficiently decreasing the time periods between two successive replications.

However, there are some deficiencies in the description of the present model which should be removed before any computational or experimental test. Most important deficiency is the absence of enzyme's state in the computations. To obtain a more realistic description, a state should be assigned to the enzyme and the whole process including **U** and **S** should leave this state invariant at the end. In 1991, a self-consistency condition for a quantum state was introduced to describe and understand a disparate interaction [11]. A similar utilization of the self-consistent states in the description of the enzymes seems to be appropriate. This is possible, even though the state of an enzyme is expected to be mixed, and that the purification of a mixed state in Deutsch's formalism [11] is impossible [39]. We note that proofs given in [39] are not valid for the mixed states which are used to describe enzymes under the self-consistency condition. We plan to investigate this further in the near future.

Finally, entanglement swapping may be a basic tool used by enzymes and proteins in the cellular environment. If so, similar models may be developed for amino acid - tRNA, aminoacyl-tRNA - mRNA, and amino acid - amino acid interactions in the protein synthesis. If successful models for these interactions can be developed, then we can achieve a deeper understanding of the role of the quantum effects and dynamics on the cellular information processing. Perhaps, entanglement swapping will join and contribute to the debates on the universal triplet genetic code [35, 36, 46] and on the mechanism behind adaptive mutation [31, 33, 34] after such models.

All in all, quantum effects are used mainly for the determination of molecular shapes, sizes and chemical affinities in molecular biology and biochemistry. Although functions of bio-molecules are explained by structure, such as the complementary geometries of molecules and weak intermolecular hydrogen bonds in nucleobase pairs, further quantum effects are not thought to play any significant role in the present biochemical complexity. However, they may be more useful tools to understand the physics of life if quantum circuits/protocols and organic molecules are considered as software and hardware of the living systems. Reconsideration of evolution as co-optimization of hardware (structure) and software (function), reconciles two opposite approaches: natural selection and self-organization. Thus, emergence of the life as a biochemical complexity may be demystified in the context of quantum information theory.

Acknowledgements

Onur Pusuluk thanks Institute of Theoretical and Applied Physics (ITAP) for the hospitality in the early stages of this work, and would like to acknowledge support from the Scientific and Technological Research Institute of Turkey (TÜBİTAK) National Scholarship Program for PhD Students.

Appendix A. Transformation V used in S

Transformation V used in **S** has thirty seven gates as shown in Figure 12. Such a number seems to be very large for an efficient replication process. However, Figure 12 is a general representation and all of the gates are not effectively used in each base pair (see Table II). In fact, average effective gate number is approximately seventeen.

TABLE II: Effective gate number of transformation V (Figure 12) for each base pair $\mathrm{N}_1 \cdot \bar{\mathrm{N}}_2$.

N_1 \ $\bar{\mathrm{N}}_2$	A	T	G	C
A	12	11	20	19
T	11	11	21	16
G	17	16	22	22
C	18	14	22	19

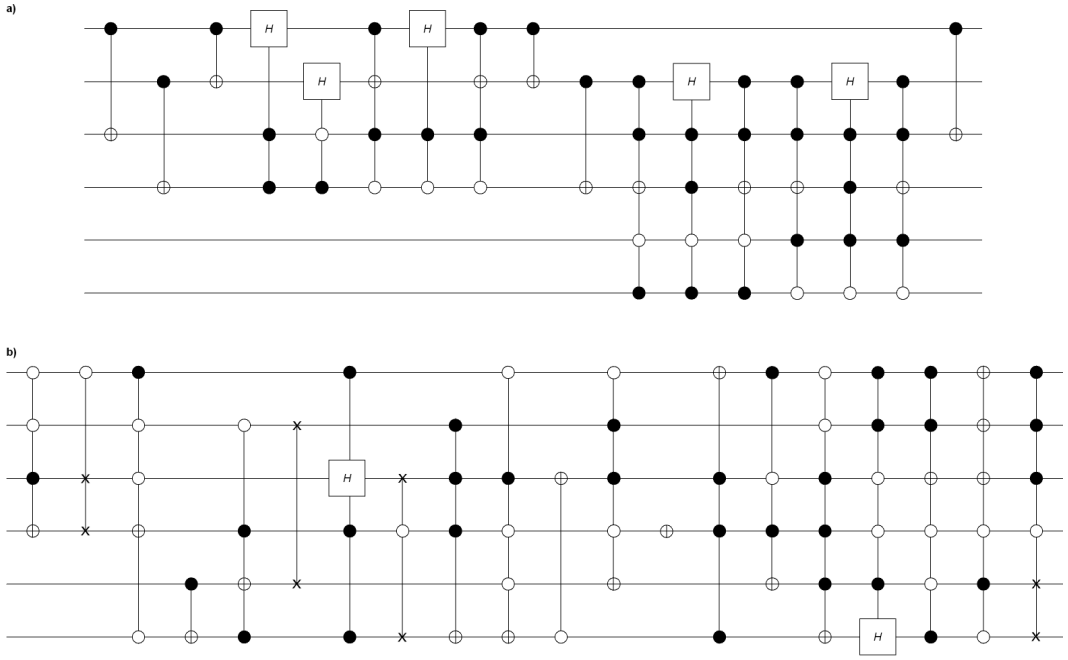

FIG. 12: Quantum transformation V used in **S**: quantum gates indicated by a double $\times$ are swap gates. *a*) First part of the transformation V which makes the states of the proper base pairs orthogonal to each other and to the states of the improper base pairs. *b*) Second part of the transformation V which converts the third qubit pair into $|01\rangle$ in G·C (or C·G) pair and into $|11\rangle$ in A·T (or T·A) pair. In the case of an improper base pairing, it produces a superposition of states in which third qubit pair is always $|00\rangle$ or $|10\rangle$.

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